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Chronic Liver Disease in Peru: Role of Viral Hepatitis

William B. Barham, Rolando Figueroa, Irving A. Phillips, and Kenneth C. Hyams

National Naval Medical Center (W.B.B.) and Naval Medical Research Institute (K.C.H.), Bethesda, Maryland; Hospitale Rebagliati (R.F.) and Naval Medical Research Institute Detachment (I.A.P.), Lima, Peru

The prevalence of antibodies to hepatitis C virus (anti-HCV) was determined in 105 patients with biopsy-proven chronic liver disease and 128 comparison patients without any evidence of liver pathology living in Lima, Peru. Using a second-generation EIA screening and supplemental immunoblot assay, anti-HCV was detected in four of 13 patients with chronic hepatitis, in 11% of 85 patients with cirrhosis, and in none of seven patients with hepatocellular carcinoma. Only two (1.6%) comparison patients without liver disease had anti-HCV. Hepatitis B surface antigen (HBsAg) was found in 23% of patients with chronic hepatitis, 12% of patients with cirrhosis, and three of seven patients with hepatocellular carcinoma. There was no evidence of chronic viral hepatitis or alcohol abuse (reported by one-third of subjects) in 48% of chronic liver disease patients. These preliminary data suggest that among this South American population neither hepatitis B nor hepatitis C infection is the predominate cause of chronic liver disease and that other infectious or environmental factors may be important. © 1994 Wiley-Liss, Inc.

KEY WORDS: hepatitis B, hepatitis C, cirrhosis, hepatocellular carcinoma

INTRODUCTION

The recent development of serologic assays for the detection of antibody to hepatitis C virus (anti-HCV) has enabled investigators to determine the prevalence of this infection in different populations. Of particular importance is the role of HCV in chronic liver disease and the relationship between hepatitis B and C virus infection [Chen et al., 1990]. Patients with chronic hepatitis, cirrhosis, and hepatocellular carcinoma have been noted in various studies to have an increased prevalence of anti-HCV. The frequency of HCV infection in these conditions has varied from population to population and has been higher in patients without chronic hepatitis B [Boonmar et al., 1990; Bruix et al., 1989; Bisceglie et al., 1991; Chang et al., 1992; Chia et al., 1991; Chuang et al., 1992; Colombo et al., 1991; Kew et al., 1990; Lai et al., 1992; Levrero et al., 1991; Poynard et al., 1991; Shimizu et al., 1992; Simonetti et al.,

1992]. To assess the role of HCV infection in chronic liver disease in Peru, we undertook a cross-sectional study to determine the prevalence of anti-HCV in Peruvian patients.

PATIENTS AND METHODS

All patients presenting at 11 different hospitals and clinics in metropolitan Lima, Peru, from October, 1991, to May, 1992, with clinical histories and physical signs consistent with chronic liver disease who required a liver biopsy were evaluated for participation in the study. A total of 105 patients who had chronic hepatitis, cirrhosis, or hepatocellular carcinoma based on needle biopsy were then included in the study after they provided informed consent. Blood samples from study patients were evaluated, whenever indicated, for serum copper, ceruloplasmin, ferritin, iron, antinuclear antibodies (ANA), and antimitochondrial antibodies to rule out nonviral causes of liver disease. Study subjects generally were from a middle-class socioeconomic background and were living predominately in the greater metropolitan Lima area.

A convenience sample of 128 patients who presented to the same hospitals and clinics during this time period without any historical, physical, or laboratory findings indicating liver disease were included in the study for comparison. Comparison patients were similar to the study patients with respect to residence and socioeconomic status and were being seen in both inpatient and outpatient settings for a variety of medical and surgical problems. A detailed history of alcohol abuse, defined as being repeatedly intoxicated at least once per week, was obtained from both liver disease and comparison patients.

Serum samples were obtained from all study subjects and were tested for hepatitis B surface antigen (HBsAg) and total antibody to hepatitis B core antigen (anti-HBc) by enzyme immunoassay (EIA, Abbott Lab-

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The opinions and assertions contained herein are those of the authors and are not to be construed as official or as reflecting the views of the Department of Defense, the Department of the Navy, or the naval services at large.

Address reprint requests to LCDR William B. Barham, Infectious Diseases Division, National Naval Medical Center, 8901 Wisconsin Avenue, Bethesda, MD 20889-5600.

TABLE I. Results of Serologic Tests for Anti-HCV, HBsAg, and Anti-HBc Among 105 Subjects With Liver Disease and 128 Comparison Subjects Without Liver Disease

Category	N	No. (%) positive			
		Anti-HCV second-generation EIA	Anti-HCV immunoblot assay	HBsAg	Anti-HBc
Chronic hepatitis	13	4 (31)	4 (31)	3 (23)	6 (46)
Idiopathic	6	0	0	0	1 (16.7)
Hepatitis B	3	0	0	3 (100%)	3 (100)
Hepatitis C	3	3 (100)	3 (100)	0	2 (66.8)
Viral hepatitis and alcohol abuse	1	1 (100)	1 (100)	0	0
Cirrhosis	85	9 (11)	9 (11)	10 (12)	34 (40)
Idiopathic	42	0	0	0	17 (40.5)
Alcoholic	26	0	0	0	8 (30.8)
Hepatitis B	4	0	0	4 (100)	4 (100)
Hepatitis C	5	5 (100)	5 (100)	0	2 (40)
Viral hepatitis and alcohol abuse	8	4 (50)	4 (50)	6 (75)	5 (62.5)
Hepatocellular carcinoma	7	0	0	3 (43)	5 (71)
Comparison patients	128	4 (3)	2 (1.6)	13 (10)	38 (30)

oratories, Abbott Park, IL). HBsAg-positive sera were also tested for antidelta by EIA (Abbott). Sera were initially tested for anti-HCV by both a first-generation EIA (Chiron Corporation, Emeryville, CA) and a second-generation EIA (Ortho Diagnostic Systems Inc., Raritan, NJ). Samples repeatedly reactive for anti-HCV by EIA were then tested by a second-generation immunoblot assay (Chiron RIBA HCV Test System). Only those specimens positive by immunoblot testing were considered anti-HCV positive for the purposes of data analysis. Proportions were compared using the χ^2 test with Yates's correction or Fisher's exact test.

RESULTS

The mean age of the 105 subjects with liver disease was 57 years (range 23–81 years); 55% were male. The mean age of the 128 comparison subjects was 55 years; 52% were male. Among the 105 patients with liver disease, 13 had chronic hepatitis, 85 had cirrhosis, and seven had hepatocellular carcinoma.

Sera from 12 patients with liver disease were anti-HCV reactive by both first- and second-generation EIAs. The serum of one patient with chronic hepatitis that was initially negative by first-generation EIA was reactive by second-generation EIA. All thirteen (12%) EIA reactive samples, including the one reactive only by second-generation EIA, were positive for anti-HCV by immunoblot assay. Anti-HCV was detected in four of 13 patients with chronic hepatitis, in 11% of 85 patients with cirrhosis, and in none of seven patients with hepatocellular carcinoma (Table I). Only two of 128 (1.6%) comparison patients without any evidence of liver disease had anti-HCV by immunoblot assay ($P < 0.001$ vs. patients with liver disease).

HBsAg was found in three of 13 patients with chronic hepatitis, in 12% of 85 patients with cirrhosis, in three of seven patients with hepatocellular carcinoma, and in 13 (10%) comparison subjects. Antidelata was found in two patients with cirrhosis. Only two study patients

who were anti-HCV positive had HBsAg. Anti-HBc was found in 43% of patients with liver disease and in 30% of comparison subjects ($P = 0.05$).

A history of alcohol abuse was found in 37% of patients with liver disease and in 22% of comparison subjects ($P = 0.03$). Thus, among the 13 patients with chronic hepatitis, six were classified as having idiopathic disease, three had hepatitis B, and four had hepatitis C. Alcohol abuse was reported by only one patient with chronic hepatitis (Table I). Among 85 patients with cirrhosis, 42 were classified as idiopathic. 26 had a history of alcohol abuse with no serologic markers of viral hepatitis, eight had hepatitis B virus infection, seven had hepatitis C virus infection, and two had dual hepatitis B and C virus infections (Table I). Alcohol abuse was reported by 47% of 17 cirrhotic patients with hepatitis B and C virus infection. Overall, evidence of viral hepatitis or alcohol abuse could account for 52% of chronic liver disease cases; 48% of subjects had no apparent cause of liver pathology.

A history of one or more blood transfusions was reported by 47% of patients with liver disease and by 17% of comparison subjects ($P < 0.001$). Among the 233 study subjects, anti-HCV and anti-HBc were found more often among subjects who had had a blood transfusion than among subjects who had not been transfused (14% vs. 3% and 51% vs. 29%, respectively; $P < 0.01$ for both comparisons). However, study subjects had often received more than one transfusion, and it was not possible to determine whether a transfusion preceded the onset of liver disease. Fifty-four percent of 48 patients with idiopathic hepatitis and idiopathic cirrhosis had a history of a blood transfusion.

DISCUSSION

The current study suggests that neither hepatitis B virus nor hepatitis C virus is the predominate cause of chronic liver disease in this Peruvian population, because evidence of infection was found in only 26% of

patients. Only among patients with hepatocellular carcinoma was hepatitis B a major factor. The low prevalence of anti-HCV-positive patients in the current study is similar to that in other Peruvian populations [Hyams et al., 1992] and is consistent with recent studies that have found anti-HCV in 7% of patients with cirrhosis [Coursaget et al., 1990] and in 15% of patients with chronic hepatitis [Boonmar et al., 1990]. However, among patients with chronic liver disease but without chronic hepatitis B, HCV infection has been found to be much more prevalent than in the current study [Chen et al., 1990; Kiyosawa et al., 1990]. Also, although the numbers were small, none of the seven patients with hepatocellular carcinoma in our study had anti-HCV, which contrasts with 11–70% of patients in other countries [Boonmar et al., 1990; Coursaget et al., 1990; Chang et al., 1992; Farinati et al., 1992; Ramesh et al., 1992; Simonetti et al., 1992].

There are several potential explanations for the low level of HCV infection in patients with chronic liver disease in this Peruvian population. First, there may be other factors responsible for the development of chronic liver disease in this population that are independent of HCV or HBV infection. Several studies have indicated that another parenterally transmitted viral infection may cause acute and chronic liver disease [Alter et al., 1992; Dasarathy et al., 1992]. An additional possibility is that the current immunoblot assay lacks sensitivity; however, this test as been shown to have a good predictive value in determining the infectivity of transfused blood [Alter et al., 1989; van der Poel et al., 1990; Ebeling et al., 1990; Skidmore, 1990; Boudart et al., 1990; Bellobuono et al., 1990], and second-generation serologic assays have detected 90% of patients with community-acquired HCV infection [Alter et al., 1992]. A final possibility is that an HCV variant not detected by current serological methods is present or that the immune response to the virus in this population is directed to antigens that are not detected with currently available tests [Alter et al., 1992].

In conclusion, it does not appear that either HBV or HCV infection is the predominate cause of chronic liver disease in Peru. These data suggest that other infectious or environmental agents present may be important factors in the development of chronic liver disease in this population [Alter et al., 1992]. While the association between anti-HCV and hepatocellular carcinoma appears to be significant in some populations, the exact role of HCV in the development of chronic liver disease and hepatocellular carcinoma in other populations remains unclear, as in this study.

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